Cholera and yellow fever, plague, etc.—Continued.

PLAGUE—Continued.

Places.	Date.	Cases.	Deaths.	Remarks.
India—*Continued.*				
Bombay	Mar. 9–Mar. 30		1,431	Estimated deaths for this same period, 2,730.
	Mar. 31–June 1		1,681	Estimated deaths from March 31 to April 20, 2,892.
	June 2–June 22		79	
Calcutta	Feb. 6–Feb. 13		1	
Karachi	Jan. 11			Plague epidemic; 220 cases, 214 deaths to date.
China:				
Amoy	June 30			Plague epidemic reported.
Hongkong	Dec. 13–Dec. 29			A few cases.
	May 21–May 29	4	2	
	June 6–June 12		1	
Macao	Apr. 1–May 31		154	
	June 1–June 3	43		
	June 1			Plague epidemic reported.
Swato	May 4			Epidemic of plague reported.
Japan:				
Formosa	Nov. 6–Nov. 30	53	37	
	Dec. 4–Dec. 29		15	
	Jan. 19–Jan. 27	3		
	Feb. 23–Mar. 12	3		
	Mar. 13–Mar. 23	4		
	Mar. 24–Mar. 31	3		
	Apr. 1–Apr. 20	64	54	
	Apr. 20–May 20	268		
	May 31–June 27	144		
Nagasaki Ken	June 9–June 27	3	3	
Taihoku	Apr. 20–Apr. 27	3		
Russia:				
St. Petersburg	Apr. 10–Apr. 17		1	
Theodosia	Mar. 31			One case of plague on Br. S. S. *Baldwin.*

BRAZIL.

Sanitary report from Rio—Sanarelli on the yellow fever germ.

RIO DE JANEIRO, *June 14, 1897.*

SIR: I have the honor to transmit report for the week ended June 12, 1897:

There were 6 deaths from accesso pernicioso, an increase of 2; none from yellow fever, 2 in the foregoing week; 2 from beriberi, a decrease of 6; 4 from enteric fever, an increase of 2; none from influenza, 1 in the foregoing week; 51 from tuberculosis, an increase of 13; and 291 from all causes, an increase of 30.

Just now the town and port are in an excellent sanitary state.

Dr. Sanarelli.—Inclosed I send a copy of Dr. Sanarelli's report of his discovery of the yellow fever bacillus. He seems to have satisfied all the professionals here of the truth of his claim, and I hope it is true, but I have outlived so many discoveries in the same line that I await confirmation. I will send you anything on the subject that transpires.

Since last report the following-named ships have been inspected or received bills of health from this office: June 7, steamship *Buffon*, British, for New York, and steamship *Sardinian Prince*, British, for New York from Buenos Ayres. June 10, bark *Jacobine*, German, for Apalachicola, Fla. June 11, bark *Pactolus*, American, for Barbados, West Indies. June 12, steamship *Biela*, British, for New York; bark *Closeburn*, British, for New York; bark *Doris Brodersen*, Danish, for

Fernandina, Fla., and barkentine *Josephine*, American, for Baltimore, Md. June 14, steamship *Kirkfield*, British, for St. Lucia, West Indies.

Respectfully, yours, R. CLEARY, M. D.,
Sanitary Inspector, U. S. M. H. S.

[Inclosure.]

Sanarelli on the Germ of Yellow Fever.

[Translated in this Bureau from the Portuguese.]

It is now four centuries since a terrible disease, then unknown to Europeans, made its appearance among the followers of Columbus.

Scarcely two centuries have passed since the same disease, spreading from its place of origin in the Gulf of Mexico and the Antilles, appeared in South America, when the epidemic of Olinda gave occasion to the Portuguese physician Ferreira de Rosa to write his treatise on the pestilential disease of Pernambuco, a new morbid process destined to become, unhappily, widely known under the name of yellow fever.

One fact is worthy of note, with other infectious diseases recorded in history as occurring in the form of epidemics, a sort of immunity has been acquired and transmitted by inheritance which has had a tendency to diminish the virulence of the disease and to restrict it within its original limits. With yellow fever, on the contrary, the prevalence and virulence of the disease have increased and show no tendency to become attenuated. Circumscribed at first to a relatively narrow zone, between the Gulf of Mexico and the Antilles, it successively and repeatedly invaded the eastern coast of the two Americas, from the Gulf of St. Lawrence to the Rio de la Plata. In more recent times it has passed the Isthmus of Panama and crossed an ocean, to appear on the west coast of America and the Atlantic littoral of Europe and Asia.

The Mediterranean Coast has not been exempt, the Strait of Gibraltar having proved an insufficient barrier against the invasion of disease, as in our day has been shown to be the case with the Suez Canal.

Indeed, it may be affirmed that as the means of communication increase no region of the globe may be expected to remain exempt from the disease now definitely installed in its classical foci, the Gulf of Mexico, the Antilles, Brazil, and Sierra Leone.

Yellow fever also shows a tendency to spread from the maritime districts into the interior, cities in which it was never previously known being now as open to attacks as Bahia and Santos. In this state of affairs, which threatens to become more serious, it is incumbent on physicians to make every effort to solve the different problems presented by this disease.

It is not sufficient to address ourselves to the clinical study of yellow fever. We must know its cause and prophylaxis. These questions can be solved only in the light of the modern science of microbiology. Hence, when by the favor of my colleagues and of the Government I was called to found the new Institute of Experimental Hygiene, my mind turned with irresistible attraction to the study of this disease.

In the charming region of the Plata, where Nature has been so prodigal of gifts, the ordinary diseases do not number as many victims as in some other countries. This is due to a combination of hygienic and social conditions. Statistics of morbidity and mortality furnish the basis of this statement. But this region is far from being exempt from invasions of yellow fever—witness the great and disastrous epidemic of 1872.

OUR PRESENT KNOWLEDGE WITH REGARD TO THE ETIOLOGY OF YELLOW FEVER.

What is the process or the pathogenic agent of yellow fever? At one time, now somewhat remote, yellow fever was believed by physicians to be due to malarial influence. Later the existence of specific microbes was admitted, and many bacteriologists devoted themselves to investigation. Of the results of these investigations, which have been for the most part negative, erroneous, and in some cases fantastic, there is no need to speak.

Dr. Sternberg, author of the most recent, complete, and adequate communication on this subject, asserts that the microbe of yellow fever is yet to be found, and that the search for it must be recommenced, *ab initio*.

In common with most authorities on this subject, Dr. Sternberg and the majority of Brazilian scientists, among whom may be cited Dr. Lacerda, agree in considering yellow fever as a local infection, having its principal seat in the stomach.

Here the infectious agent, as yet undetermined, is supposed to elaborate its toxic

substances, whose absorption by the blood gives rise to the peculiar characteristics of yellow fever.

Following out this theory, Sternberg and the other authorities mentioned, advise the treatment of yellow fever with alkaline remedies and intestinal disinfectants.

THE TRUE ETIOLOGY—THE ICTEROID BACILLUS.

The clinical, etiological, and epidemiological theories of yellow fever had reached this point when I began to devote my small abilities and the means placed at my disposal by the University of Montevideo to the direction of the Institute of Experimental Hygiene.

The material for my studies was procured partly from the lazaretto on Flores Island, where, during the summer months, a small laboratory is maintained, designed for the study of living subjects and cadavers of persons arriving from Brazil and taken ill en route; in part, from the hospital of St. Sebastian, where, thanks to the courtesy of Dr. Seidl and Drs. Fajardo and Couto, I was enabled to install myself conveniently and devote myself for more than a month to anatomical, bacteriological, and clinical research. My studies covered a ground encumbered with many difficulties.

The recognition and isolation of the specific agent of yellow fever may be considered as not the least difficult task presented to the patient microbiologist. This explains the ill success of those who have preceded me in this line of investigation.

No one who has followed a case of yellow fever, and observed the successive development of the symptoms which give this disease its marked and peculiar character, can doubt for an instant that the process is due to the action of a microbe which is absolutely specific, and which can be easily demonstrated in necropsy. In the majority of cases, however, the most complete and minute bacteriological investigation of the cadaver seems calculated to mislead the investigator and turn him from his purpose.

The bodies of icteroid typhus (yellow fever) patients will be found to be invaded by certain microbic species, streptococci, staphylococcus, pyogenes, coli bacillus, etc., which are in no way responsible for the disease, or they are invaded by a mixture of microbes, the classification of which is a stupendous undertaking.

I do not think it necessary to indicate here the method of my discovery of the microbe of yellow fever. I will only say that the discovery was made in the second case observed at Flores Island. This case, unlike the first, which presented a mixture of microbes, showed the bacillus in a state of relative purity. This bacillus may, with all propriety, be termed the icteroid bacillus, since yellow fever is also termed icteroid typhus. I say "in a state of relative purity" because yellow fever is the prototype of diseases due to infection from mixed microbes. In the 11 necropses performed by me I never found the icteroid bacillus isolated. It was always associated with the bacillus coli, the staphylococcus, or the streptococcus. In the second case at Flores Island it was associated, in small quantity, with the bacillus coli, and in the eighth, studied at Rio de Janeiro, with the staphylococcus aureus.

I will here state that the icteroid bacillus should be sought in the blood or tissues, and not in the gastrointestinal cavity, contrary to what might be presumed *a priori* in the premises. In fact, in yellow fever, the digestive canal is the seat, as in typhoid fever, of an abundant germination of bacillus coli, which is there found in a state of absolute purity.

The results of my investigations show that the icteroid bacillus may be isolated in 58 per cent of the cases of yellow fever, and in some cases may be found even during life. The reasons why it may not always be recognized are easy of comprehension. In the first place, the icteroid bacillus multiplies very slowly in the first stage of the disease, a very small quantity of the toxin being sufficient to develop in the human subject a very grave case of yellow fever. In the second place, the toxin, either of its own potency or by means of the profound lesions which it determines in the digestive fluids and the liver, facilitates to the most extraordinary degree secondary infections of every sort. These secondary infections may some times assume the type of true septicæmia, due to bacillus coli, to streptococci or staphylococci, etc., and are sufficient of themselves to cause death. At other times they occur in such multiple colonies as to transform the patient into a veritable culture of all the species of intestinal microbes. Finally, as the result of my observation that the icteroid bacillus always occurs in the blood and tissues and not in the gastrointestinal contents, we may conclude, contrary to what has hitherto been received, that the virus of yellow fever does not reside in the intestinal tube, and that its toxin, instead of being absorbed by the intestinal walls, is elaborated in the interior of the organs and in the blood.

This bacillus, morphologically considered, never presents marked characteristics at the first view. It is a small rod with rounded extremities, generally united in pairs

in cultures, and in small groups in the tissues, from two to four thousandths of a millimeter in size, and generally two or three times longer than it is wide. It is sufficiently pleomorphous.

Investigation of the tissue gave good results when the death of the patient occurred without secondary septicæmia. But even in cases in which bacteriological results are most pure it is not always easy to verify them when the tissue is under observation on account of excessive exudation. Aside from this, however, by observing correct methods we may expect to encounter these organisms in small groups, preferably in the lesser capillaries of the liver, etc.

The best means of demonstrating not only its existence, but even its special tendency to localize itself in small groups, principally in the blood capillaries, consists in cutting off a piece of liver taken from a fresh cadaver, and kept in a stove (thermostat) for twelve hours to facilitate the multiplication of specific microbes.

The bacillus of yellow fever develops well in all the ordinary culture media. In ordinary gelatin cultures it forms rounded, transparent, and granular colonies, which during the first three or four days present the appearance of leucocytes.

The tendency to granulation becomes constantly stronger and ordinarily there is formed a central nucleus which is completely opaque. In time the colonies become entirely opaque without liquefying the gelatin.

In streaked gelatin, obliquely solidified, it develops in the form of small brilliant drops, resembling milk in their opacity. In meat broth it develops weakly, without forming either pellicles or flaky deposits. In solidified blood serum its growth is almost imperceptible.

Culture of gelose (agar-agar), contrary to what has been observed for the majority of the recognized pathogenic microbes, furnishes for the icteroid bacillus a diagnostic of the first order. This diagnostic value can, however, be relied on only under definite conditions.

When the colonies develop in the incubator they assume an aspect not unlike that of many other microbes. They are rounded, ashy, iridescent, transparent, with smooth surface and regular margins.

If instead of being developed in stove heat at a temperature of 37° they are grown at the temperature of the surrounding air, 20° or 22°, the colonies form as before, milky, opaque drops, with a mother-of-pearl luster, entirely different from the colonies developed in the stove incubator. We may utilize this difference in the mode of development, exposing the culture first to a stove incubator temperature for from twelve to sixteen hours, and then keeping it for another twelve or sixteen hours at the ordinary temperature. The colonies will then be seen to consist of a flat central nucleus, transparent and bluish, and with a circular periphery very pronounced and opaque, exactly resembling an impression in sealing wax. As this characteristic, which may now be considered specific, may be put in evidence in about twenty-four hours, it serves to determine, in the most rapid and certain manner, the bacteriological diagnosis of the icteriod bacillus. In addition to these morphological characteristics, which serve to differentiate the microbe of yellow fever from all other species now known, the icteroid bacillus is endowed with some interesting biologic properties. It is a facultative anærobe, does not resist gram coloration, ferments insensibly in glucose and saccharose, but is not capable of coagulating milk ; resists fermentation, dies in water at 60°, succumbs in seven hours to the action of solar rays, and lives some time in sea water.

The specific microbe of yellow fever is pathogenic for the majority of domestic animals.

There are few microbes whose domain is so extended and varied. Although birds are completely refractory, all the mammals which have been subjected to experiment show themselves to be more or less sensitive to the pathogenic action of the icteroid bacillus. It kills white mice in five days, causing general septicæmia with fatty degeneration of the liver. In the guinea pig it determines, alike in small and large doses, a cyclic febrile affection, which always terminates in death in from eight to twelve days. Infection may be produced by any method, even through the respiratory system.

As soon as introduced into the organism the microbes collect, for the most part, in the spleen, where they remain during the entire evolutionary period of the disease without any notable increase. At the end of six or seven days they suddenly invade the circulation, enter upon a period of proliferation, and kill by septicæmia.

The anatomical lesions which are found in necropsy are represented by hypertrophy of the thymus gland, by splenic tumors, by axillary and inguinal adenitis, and by hepatic lesions only in chronic cases, which are very rare.

Less frequently adenitis, nephritis, and albuminuria are encountered ; also, very rarely, serous hæmorrhages.

The rabbit is rather more sensitive than the guinea pig to the action of icteroid virus. Whatever be the dose and by whatever means introduced, it infallibly kills after a

periodic affection lasting four or five days if by subcutaneous inoculation, in two days only if the inoculation be made directly in the blood.

The process of evolution of the infection in this case is precisely similar to the same process in guinea pigs.

The anatomical lesions are represented in the guinea pig by splenic tumor; by hypertrophy of the thymus gland and by adenitis, as has been said, the icteroid virus is capable of determining in rabbits, nephritis, enteritis, albuminuria, hemoglobinuria, and various haemorrhagic manifestations in the serous cavities. But the animal which lends itself better than any other to the production of the anatomical and symptomatic manifestations of experimental and human yellow fever, is the dog. The inoculation should be intravenous. The morbid process which results, manifests itself almost immediately and with such violence of symptoms and complication of lesions as to recall the clinical and anatomical features of human yellow fever. The first marked symptom in the development of experimental yellow fever in the dog is the vomit, which occurs as soon as the virus has reached the blood, and continues a long time, as if the animal were under the influence of a strong emetic. After the vomit come enterorrhagias; urine is slight and albuminous, and soon manifests the anuria which immediately precedes death. In one case I observed grave icterus. The necropsy shows extremely interesting lesions, being almost identical with those observed in human cadavers. Especially notable is the presence of steatoma of the liver.

The hepatic cells, examined fresh, with a little osmic acid, appear completely degenerated and enlarged, as in the case of human beings who have died of yellow fever. The virus of yellow fever is, indeed, as will be shown later on, a genuine specific poison of the hepatic cell, similar to phosphorus or arsenic.

Complete steatosis of the liver may be determined by injecting into that organ, directly through the abdominal walls, a fresh culture of the specific bacillus.

Beside the liver, the renal tissue presents grave fatty degeneration. This tissue is the seat of an acute parenchymatous nephritis, which may be considered the immediate cause of the anuria and uremic poisoning. In fact, the blood of dogs, dead of experimental yellow fever, contains a large quantity of urea, equal to that found in the blood of human beings affected with nephritis, or in very grave cases of human yellow fever.

The entire digestive apparatus is the seat of a gastroenteritic hemorrhage of the gravest imaginable character, only comparable to that which is provoked by poisoning with cyanide of potassium. This haematogenous gastroenteritis is therefore perfectly analogous to, but much graver than that which is observed in man.

The final peculiarity observed gives great interest to yellow fever produced in dogs, and is a bacteriological result. In the majority of cases the icteroid bacillus is found in the blood, and in the organs in variable quantity, but not in a state of absolute purity. Sometimes it may be found associated, as in man, with the bacillus coli or streptococcus. In view of this tendency to invasion by secondary microbes, which we find in dogs in which yellow fever poisoning has been induced, and in filtered cultures of the bacillus, we may conclude that yellow fever virus, whether of itself or in consequence of the alterations which it causes in the various viscera, especially in the liver, which was supposed to be a defence against microbes, is favorable in the dog to secondary infections, frequently having their point of departure in the intestinal canal. This constitutes an important point of bacteriological contact between yellow fever in the dog and in man. In one case observed the liver was completely transformed to a fatty mass, resembling wax.

The experiments made on monkeys are of great interest, because they demonstrate the possibility of obtaining in these creatures a fatty degeneration of the liver even more grave than that observed in man.

In Simians, as in dogs and human beings, the affection frequently terminates with bacteriological products of a mixed infection of staphylococcus and streptococcus.

Goats and sheep are also very sensitive to icteroid virus, and the same conjunction of phenomena occurs in these animals which we have observed in our other investigations in comparative pathology. In fact, beside the grave fatty alteration of the liver, which never fails, nephritis, anuria, uremic poisoning, and mixed infection are observed.

YELLOW FEVER AND SECONDARY INFECTIONS—RAPID BACTERIOLOGICAL DIAGNOSIS OF THE ICTEROID BACILLUS.

Yellow fever is an infectious disease, due to a microorganism which is well defined and susceptible of being cultivated in ordinary nutritive media. This microorganism, which was provisionally designated *icteroid bacillus*, may be isolated not only in the cadaver, but also during the life of the yellow-fever patient. Its isolation often presents almost insuperable difficulties, due in part to the constant intromission of secondary infections and in part to its relative scarcity in the organism.

The secondary infections, due almost always to specific microbes already determined, as the staphylococcus, streptococcus, bacillus coli, proteus, etc., may invade the patient some time before death, and it can not be denied that the death of the patient may some times be more justly imputed to their action than to that of the icteroid bacillus.

It is probable that one of the causes which impress a protean character on yellow fever is due to the nature and evolution of these secondary infections.

Yellow fever, both in man and the lower animals, represents a disease of cyclic progress. During this period the specific microbe is found in the organs in a state of great scarcity, and it is in the morbid period, or after seven or eight days, that it suddenly invades the whole organism, accompanied almost invariably by other microbes of intestinal origin. It is only in cases that terminate in this way—that is to say, in those which execute a regular cyclic development—that the specific microbe may be readily found dispersed throughout the blood and the organs.

When intercurrent septicæmia and premature uremic poisoning abruptly terminate this morbid period, the isolation of the icteroid bacillus is extremely difficult, if not impossible.

The icteroid bacillus once introduced into the system, not only determines a general infection, but causes specific alterations, having their favorite location in the kidneys, in the digestive canal, and the liver. In the last-named organ a rapid fatty degeneration takes place, in the digestive canal gastroenteritis, and in the kidneys, acute parenchymatous nephritis.

The yellow-fever patient is, in fact, menaced by three imminent dangers, and examination of the cadaver may determine the immediate cause of death.

1. Death may be considered due in great part to specific infection, particularly when the icteroid bacillus is found in the body in considerable quantity and in a state of relative purity. This occurs in cases which complete the full morbid cycle.

2. It may be considered as produced by septicæmias successively established during the course of the disease when the cadaver shows products of almost pure cultures of other microbes.

3. It may be due in great part to insufficient action of the kidneys, when the body is found almost sterile with a considerably large quantity of urea in the blood, death having occurred before the morbid cycle had completed its evolution.

It is difficult to pronounce during the life of the patient on the predominance of specific uremic symptoms, because the most salient features of yellow-fever poisoning are easily confounded with failure of the kidneys. This frequent and unavoidable complication is sometimes the principal cause of the failure of yellow fever to take on a distinctly thermic type.

It is very probable that certain temperatures, which are apparently normal, and certain low temperatures, which manifest themselves very frequently during the period of delirium and in full convalescence and some sudden and unexpected terminations of the morbid process, are for the most part due not to the action of yellow-fever poison, but to uremic poisoning.

The symptom called *black vomit* is caused by the action of gastric acidity on the blood, which escapes into the stomach through the lesions in the mucous membrane.

The act of vomiting is caused directly by the specific emetic action of the icteroid bacillus circulating in the blood.

The hæmorrhagic character presented by the disease is due, primarily, to the hæmorrhagic property which the icteroid bacillus possesses in common with other microbes, and in the second place to the profound and rapid alterations and degenerations which it produces in the walls of the blood vessels.

The icteroid bacillus possesses morphologic characteristics so marked as to differentiate it distinctly from other microbes. Once isolated from the cadaver or the patient, its exact bacteriological diagnosis does not require more than twenty-four hours.

The icteroid bacillus is pathogenic for most of the domestic animals.

In mice, guinea pigs, and rabbits it reproduces a cyclic disease analogous to that observed in man, the duration being, in the case of the first, five days; in the second, from eight to twelve days, and, for the third, about five days. During the progress of the disease the microbes introduced by inoculation multiply sparingly in the interior of the organs. It is only twenty-four or forty-eight hours before death that they suddenly invade the circulation of the blood, killing the animal by septicæmia. The disease may be communicated through the respiratory system.

In dogs the icteroid bacillus produces anatomic and symptomatic features precisely analogous to those observed in man, viz: Hematuria, albuminuria gastroenteritis, nephritis, jaundice, deep fatty degeneration of the liver, uremic poisoning, and secondary infections.

In monkeys it produces a cyclic disease with complete steatosis of the liver, mixed infection, etc.

In goats and sheep it attacks the kidneys, causing albuminuria and uremic poisoning. It also produces acute specific degeneration of the hepatic cell and favors mixed infection. The virus of yellow fever possesses, therefore, three series of pathogenic properties, which in conjunction give it its peculiar character and entitle it to be considered specific.

1. Steatogenic properties, which manifest themselves with intensity, the greater when the animal ranks high in the zoological scale. They are least marked in the rabbit, and attain their maximum intensity in the dog, in monkeys, and in man. To the icterus, which generally manifests itself when the disease is somewhat advanced, are due in great part, but never entirely, the grave anatomic alterations of the liver, amounting to a genuine mechanical obstruction preventing the free passage of the bile and favoring its reabsorption by the lymphatic system.

2. Congestive and hæmorrhagic properties, which, although common to various other species of microbes, yet constitute a very salient characteristic, blood vomiting, hemorrhage of the mucous membrane, and congestion of the vascular system being marked symptoms of yellow fever.

3. Emetic properties, which, although not strictly specific manifestations of yellow fever, like those last mentioned, develop with rapidity and intensity in man and the higher animals (dogs), and impress on this virus a pathogenic character.

THE ICTEROID TOXIN.

The scarcity of the icteroid bacillus in the human organism, and the violence of the symptoms which immediately manifest themselves in the dog after relatively small intravenous injection, would lead us to infer the existence of a very active specific microbe.

We will now examine this virus, which is obtained, like that of diphtheria, by simply filtering cultures of the bacillus grown in broth twenty to twenty-five days.

The virus of yellow fever will support with impunity a temperature of 70 degrees, but at the boiling point it becomes sensibly attenuated.

If, instead of filtered cultures, we take cultures sterilized with ether, the toxic power is found to be much greater. I studied the action of this virus on guinea pigs, rabbits, dogs, cats, goats, donkeys, horses, and men. It exhibited slight action and characteristics in animals which had shown themselves to be endowed with a very slight reactive power to the live virus. These were the small rodents in which death could be induced only by large doses of the virus. Small doses determined only, in general, a temporary emaciation. In the case of the dog, however, the toxin introduced intravenously produced the same symptoms and the same lesions as were described with the experiments made with virus. Immediately after injection the animal presented no particular symptoms, but ten or fifteen minutes later a general chill set in which lasted uninterruptedly and was followed by violent vomiting, at first of food and finally of mucus, until the animal had almost completely emptied the gastric cavity and lay collapsed in his cage.

In many cases premature hæmaturia was observed.

With a moderate dose the dog recovered promptly, as from an attack of poisoning produced from a vomitive agent. If, however, the dose was tolerably large, or repeated on successive days in gradually increased quantity, the dog succumbed, presenting the same anatomical lesions described as due to the action of living virus. These lesions consist of abundant hæmoglobinic exudations in the pleuras, of intense fatty degenerations of the liver, of acute parenchymatous nephritis, of albuminuria hæmaturia, and gastric hæmorrhages.

The bacteriological products are also very interesting, since they demonstrate the existence of mixed infections, due, according to the case to bacilli coli, streptococci or staphylococci.

The cat is very resistant to the action both of the virus and the icteroid toxin. Formidable doses of each may be administered without obtaining other results than a slight diminution of weight followed by slight inflammatory processes at the point of inoculation. This animal should, therefore, be considered the most resistant of all animals yet experimented on, and consequently of no present use in the experimental study of yellow fever.

Icteroid toxin presents in the goat exactly the same lesions with the exception of vomit, which I have described in dogs and men.

In the goat the tendency to hæmatolysis and the extreme sensibility of the kidney to yellow fever toxin are especially notable. The death of the animal is due in great part to the deep lesion of the viscera, while a notable quantity of urea found in the secretions of the organism is presumptive evidence of grave uremic poisoning.

I made only one experiment on a donkey. The same symptoms manifested them-

selves which have been already described, that is to say, inflammatory processes and degenerations of the liver, lesions of the mucous membrane, hæmorrhages of the parenchyma, and the serous cavities in the mucosa and the glandular system, and finally, uremic poisoning.

We now come to the action of the toxin on the horse. This animal is ordinarily sensitive even to injection of small quantities of toxin. It may be said, in general, that the higher the animal's position in the zoological scale the greater the sensibility to this virus. Subcutaneous injection even of small doses of filtered culture always causes strong local tumefaction followed by fever, which lasts from twelve to twenty-four hours. This tumefaction is painful and slow to disappear. When the quantity is much greater, or when, instead of filtered cultures, cultures sterilized with ether, which are much stronger, are used, the tumefaction is very great and is followed by widespread subcutaneous œdema, which extends from the lower part of the stomach to the limbs and for several days impedes the movements of the joints. Sanguineous ulcers, difficult to cure, are formed on the surface of the skin. The animal frequently manifests an almost continuous fever. Intravenous injection is borne much better, but still causes grave inconveniences. After each injection the animal shows a strong access of dyspnœa and is attacked by a general tremor, which obliges him to lie down on the ground. Fever ensues and the animal is prostrated for some time. On the following day, however, the temperature returns to the normal and no symptoms present themselves.

In the course of my experiments I lost several horses. One of these was a creole horse, which is much less resistant than the mixed breed to toxin in general, especially to diphtheria and yellow fever. Necropsy of this horse showed tumefaction of the spleen, nephritis, albuminuria, and some foci of enteritis.

I do not consider it necessary to dwell longer on these experiments, first, because the results were a reproduction more or less attenuated of the lesions studied with virus; secondly, because it appears to me better to demonstrate definitively the special functions of yellow fever toxin in direct experiment on the human race.

[To be continued.]

CANADA.

Smallpox in Montreal.

MONTREAL, *July 16, 1897.*

SIR: The present status of smallpox in this province is as follows:

Montreal City (population, 240,000).—Date of outbreak, July 2; cases since outbreak, 3; died, 1; still sick, 2; houses infected, 2; houses still infected, 1 (the civic hospital).

The new patient is a brother to one of the two previously reported to you on July 5.

Precautions taken.—Redisinfection of premises after removal of patient to civic hospital.

Yours, respectfully, ELZÉAR PELLETIER,
Secretary Board of Health of the Province of Quebec.

CUBA.

Smallpox and yellow fever in Cuban seaports.

July 13: The United States consul at Cardenas reports that during the week ended July 10 there were in that city 3 cases of yellow fever and 1 death from smallpox.

July 12: The United States consul at Cienfuegos reports that during the week ended July 11 there were in that city 6 deaths from, and a few cases of yellow fever.

July 17: The United States sanitary inspector at Habana reports that during the week ended July 15 there were in that city 40 deaths from yellow fever and no deaths from smallpox.